

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 52-59 and 61-68 and 71-78 are pending in the application, with claims 52 and 75 being the independent claims. Claims 69 and 70 have been canceled.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider and withdraw the outstanding rejections.

***Claim Rejections Under 35 U.S.C. § 102(b)***

Claims 52-59, 61-63, and 66-78 were rejected as anticipated by Boyd, et al. Applicants traverse this rejection.

Claims 71-78 recite methods for synthesizing nucleic acid molecules having two or more site-specific recombination sites, where the two or more site-specific recombination sites do not recombine with each other. The Boyd reference teaches only the synthesis of nucleic acid molecules having recombination sites that DO recombine with each other (*see e.g.*, the trimolecule hybrids of Figure 2, having two lox sites). Thus, the Boyd reference does not anticipate claims 71-78. Applicants respectfully request that the §102 rejection of these claims over the Boyd reference be withdrawn.

Claims 52-59 and claims 61-68 recite methods that involve first contacting a linear nucleic acid with an adapter having a first site-specific recombination site to make

an “adapterized” nucleic acid having one or more adapters at one or more termini (*see*, step (b) of claim 52), and then recombining the “adapterized” nucleic acids with a vector having a second site-specific recombination site (*see*, step (c) of claim 52). Step (c) of the recited methods results in the intermolecular recombination between the first and second site specific recombination sites. The Boyd reference teaches only INTRAMOLECULAR recombination of linear nucleic acid molecules. Figure 2 of the Boyd reference illustrates the intramolecular recombination of a trimolecule hybrid as the two lox sites of the trimolecule hybrids are acted upon by Cre recombinase to form a circular recombinant plasmid. Thus, the Boyd reference does not anticipate claims 52-59 or claims 61-68. Applicants respectfully request that the §102 rejection of these claims over the Boyd reference be withdrawn.

In view of the cancellation of claims 69 and 70, their rejection under 35 U.S.C. § 102(b) is rendered moot.

#### **Claim Rejection Under 35 U.S.C. § 103(a)**

Claims 61-65, 69-72, 74-76, and 78 were rejected as being unpatentable over Boyd, in view of Alonso. Claims 59, 61-62, 71-73, and 75-77 were rejected being unpatentable over Boyd, in view of Waterhouse. Applicants respectfully traverse these rejections.

Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. See *In re Royka*, 490 F.2d 981, 180 USPQ 580

(CCPA 1974). Absent a showing of such motivation and suggestion, *prima facie* obviousness is not established. See *In re Fine*, 5 USPQ2d at 1598. A prior art reference must be considered in its entirety, *i.e.* as a whole, including portions that teach away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). The Court of Appeals for the Federal Circuit further instructed that “references that teach away cannot serve to create a *prima facie* case of obviousness” (*In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994)), and that an “applicant may rebut a *prima facie* case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect” (*In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997)).

Claims 52-68 recite methods that involve the intermolecular recombination between an “adapterized” linear nucleic acid and a vector. Similarly, claims 71-78 recite methods for making nucleic acid molecules having two or more site-specific recombination sites that do not recombine with each other.

The teachings of the Boyd reference are directly opposite the presently claimed inventions. Boyd teaches the synthesis of “trihybrid molecules” having recombination sites that DO recombine with each other. These trihybrid molecules are specifically constructed for INTRAMOLECULAR recombination. The intramolecular recombination methods disclosed in Boyd are 180-degrees different from the INTERMOLECULAR recombination methods recited by claims 52-68. The trihybrid molecules disclosed in Boyd are specifically designed and are suitable only for intramolecular recombination, and cannot be used for the intermolecular recombination

methods recited by claims 52-68. Boyd's trihybrid molecules are specifically designed for intramolecular recombination, and are fundamentally different from the molecules recited by claims 71-78, which have recombination sites that DO NOT recombine with each other and are specifically designed for intermolecular recombination. The intramolecular recombination reactions disclosed by the Boyd reference cannot be performed using the nucleic acid products of the methods recited by claims 71-78.

In view of the above remarks, it is clear that the Boyd reference teaches away from the presently claimed invention. Accordingly, as instructed by The Court of Appeals for the Federal Circuit, the Boyd reference cannot serve as the basis for a proper §103 rejection. Neither the Alonso nor the Waterhouse references may be used to cure this defect.

In view of the cancellation of claim 70, its rejection under 35 U.S.C. § 103(a) is rendered moot.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a).

*Conclusion*

All of the stated grounds of rejection have been properly traversed. Applicants therefore respectfully request that the Examiner reconsider and withdraw all presently outstanding rejections. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,



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Date: April 11, 2006